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A nonlinear model of newborn EEG with nonstationary inputs

N.J. Stevenson, M. Mesbah, G.B. Boylan, P.B. Colditz, and B. Boashash

Abstract

Newborn EEG is a complex multiple channel signal that displays nonstationary and nonlinear characteristics. Recent studies have focussed on characterising the manifestation of seizure on the EEG for the purpose of automated seizure detection. This paper describes a novel model of newborn EEG that can be used to improve seizure detection algorithms. The new model is based on a nonlinear dynamic system; the Duffing oscillator. The Duffing oscillator is driven by a nonstationary impulse train to simulate newborn EEG seizure and white Gaussian noise to simulate newborn EEG background. The use of a nonlinear dynamic system reduces the number of parameters required in the model and produces more realistic, life–like EEG compared with existing models. This model was shown to account for 54% of the linear variation in the time domain, for seizure, and 85% of the linear variation in the frequency domain, for background. This constitutes an improvement in combined performance of 6%, with a reduction from 48 to 4 model parameters, compared to an optimised implementation of the best performing existing model.

Index Terms

newborn, neonate, EEG, modelling and simulation, nonlinear, Duffing oscillator, nonstationary,

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I. Introduction

The electroencephalogram (EEG) measures the electrical activity of the brain and is used in neonatology to assist in the diagnosis of conditions such as hypoxic–ischaemic encephalopathy, meningitis and stroke, and can be used to predict the neurodevelopmental outcome of the newborn [16], [18].

From the signal analysis point of view, newborn EEG is generally understood to be composed of a stochastic or chaotic background with a time–varying spectrum from which several deterministic patterns, such as seizure and delta brushes or modulations, such as tracé discontinu and tracé alternant, emerge [20], [21], [25]. The type of waveform and its prevalence in the newborn EEG are related to the gestational age of the newborn [20]. The newborn EEG is often contaminated with environmental artifacts, such as 50Hz or 60Hz noise and electrode noise, and interference from physiological signals, such as the EOG, EMG and ECG [17]. The structure of newborn EEG can, therefore, be summarised according to Fig. 1.

An important condition that presents on the newborn EEG is seizure. Seizure is a sign of central nervous system (CNS) dysfunction that is caused by an imbalance between the inhibitory and excitatory influences in the brain [16]. The newborn is more susceptible to such imbalances compared to the adult due to enhanced cellular excitation, synaptic excitation and propagation [16]. Seizure is primarily diagnosed in the neonatal intensive care unit (NICU) with the EEG, as clinical manifestations are often subtle, suppressed, or even nonexistent [2], [17]. The manifestation of newborn seizure on the EEG has been defined as *a clear ictal event characterized by the appearance of sudden, repetitive, evolving, stereotyped waveforms that have a definite beginning, middle and end, and last for a minimum of*

10 seconds [2]. This waveform emerges from a background EEG that consists of *mixed frequency content* [20].

Recently, the detection of newborn EEG seizure has been automated to assist the neurophysiologist when diagnosing long recordings of EEG, [1], [9], [11], [12], [19], [27]. Current techniques, although constantly improving, lack the necessary accuracy that is required for clinical implementation. This is because the characteristics of newborn EEG are not yet comprehensively defined and current methods are not robust in the presence of noise and artifacts. Improvements in both artifact removal and the analysis of the signal characteristics present in newborn EEG waveforms should result in more accurate newborn EEG seizure detection algorithms.

Several attempts have been made to accurately model the newborn EEG as such models can *(a) provide the possibility for testing the influence of different types of inputs upon the output of the system or of changing some of the properties of the constituting elements or (b) allow the formulation of hypotheses concerning new elementary properties, relationships and overall behaviour* [20]. Importantly, for the signal analyst, a comprehensive model of newborn EEG can assist the development of new features for automated methods of newborn EEG analysis such as newborn EEG seizure detection. The ability to simulate newborn EEG can also be useful. The intense effort required in obtaining large, annotated, clinical databases and the protection which is afforded such databases makes comparisons between available seizure detection algorithms difficult. Realistic simulated EEG can be used as an initial test signal for, and provide a database for the comparison of, newborn EEG seizure detection algorithms. These data can also be used for calibrating new EEG machines and when patient confidentiality and ethical limitations prohibit the use of real newborn EEG.

To the best of the author’s knowledge, the first attempt at modelling newborn EEG for seizure detection was performed by Roessgen *et al.* in [27]. The Roessgen model was a modified version of the adult EEG model proposed by Lopes da Silva *et al.* in [15]. Roessgen *et al.* added a stationary sawtooth input to Lopes da Silva’s model to simulate seizure and used linear approximations to the original nonlinear functions. The Roessgen model produces a coloured background spectrum but was unable to produce the wide range of nonstationary seizure waveforms that are known to be present on the newborn EEG as shown in [5]. The model of Celka and Colditz proposed the use of two different Wiener filters (a linear system followed by a nonlinear function) to simulate seizure and background [6]. The Celka model included a nonstationary sawtooth input, with a piecewise linear instantaneous frequency law, to account for the time–varying nature of the newborn EEG seizure waveform. The Celka model offered two important improvements in newborn EEG modelling, namely, the inclusion of the nonlinear mapping function originally outlined in [15] and the inclusion of a nonstationary input based on analysis of the seizure waveform [5]. This model was, however, still unable to model the various morphologies of the seizure waveform due to a lack of variability in the nonlinear function. These models are also impossible to implement as the range and distribution of possible inputs and model parameters used in the models are unknown. This means that newborn EEG simulation can not be performed using these models.

An alternate approach to newborn EEG modelling was presented by Rankine *et al.* in [25] (the Rankine model). This model was based on findings that the seizure waveform could be represented as a multicomponent signal with a piecewise linear instantaneous frequency (IF) law while the background waveform was modelled as a random signal with a time–varying spectrum based on an inverse power law [5]. The advantage of this approach was that it could be used to simulate newborn EEG as a range and distribution of model parameters was supplied. The random selection of a large number of model parameters, however, failed to account for dependance between parameters which meant that many seizure waveforms generated by the model were not representative of real newborn EEG seizure.

The aim of this paper is to present an improved model of newborn EEG that is capable of reproducing more realistic, life–like newborn EEG, with a minimal set of parameters, compared to existing models. The proposed model is based on a nonlinear dynamic system that is driven by stationary white Gaussian noise to simulate the newborn EEG background component and driven by a nonstationary impulse train to simulate the newborn EEG seizure component. The component nonlinear dynamic systems use different values to best represent seizure and background, respectively. The outputs of these model components are combined, via addition, to simulate newborn EEG. We begin by defining the seizure and background components of the model and then we compare these sub–models to existing models using measures of the goodness of fit between potential model outputs and real newborn EEG randomly selected from a large database of newborn EEG recordings. The range and distribution of model parameters are estimated and assumed to be random; this assumption is tested using a cross–fold validation procedure. Finally, an algorithm for simulating newborn EEG is presented.

II. Data Acquisition

The EEG data were acquired at the NICU of the Royal Brisbane and Women's Hospital, Brisbane, Australia, using the MEDELEC Profile System (Medelec, Oxford Instruments, UK). The EEG recordings were undertaken with 12 Ag/AgCL electrodes, primed with conductive gel, fixed with adhesive and placed according to the international 10–20 standard. These 12 electrodes were used to construct a 20 channel bipolar montage. The EEG was filtered with an analog bandpass filter, cutoff frequencies at 0.5Hz and 70Hz, and sampled at 256Hz. The data were then resampled to 32Hz, with digital anti–aliasing filters, as the significant energy in newborn EEG ($> 95\%$) does not exceed the alpha band (8–12Hz) [25]. A total of 30.8 hours of EEG were recorded, within 14 days of birth (mean of 4 days), from 63 term newborns. The newborn EEG was then annotated by a neurophysiologist from the Royal Children's Hospital, Brisbane, Australia. The database contains 26.5 hours of newborn EEG background and 4.3 hours of newborn EEG seizure. The seizure EEG consists of 127 seizure events with a median duration of 57 seconds and a range of [10, 1045] seconds. A set of 2000, 8 second epochs of newborn EEG background and a set of 200, 8 second epochs of newborn EEG seizure were randomly extracted from this database to test the proposed model. Example seizure and background epochs are shown in Fig. 2. All data were acquired after ethical approval had been received from the ethics committees of the Royal Brisbane and Women's Hospital and the University of Queensland, Australia.

III. NEWBORN EEG MODEL

The core of our proposed newborn EEG model is the nonlinear dynamic system [4],

$$m\ddot{x}(t) + c\dot{x}(t) + g(x(t)) = F(t). \tag{1}$$

where $g(x(t))$ is a nonlinear function that displays odd symmetry, that is $g(-x(t)) = -g(x(t))$. In keeping with a mechanical analogy, $\ddot{x}$ is acceleration, $\dot{x}$ is velocity, x is displacement, $F(t)$ is the forcing function and the derivatives are with respect to time, t. In the context of the newborn EEG model, $x(t)$ represents the recorded EEG voltage.

In the proposed model, we simulate newborn EEG seizure and background with a Duffing oscillator which is a type of nonlinear dynamic system where the nonlinearity is defined as [31],

$$g(x(t)) = k_1 x(t) + k_2 x^3(t). \tag{2}$$

This nonlinearity simulates a hardening spring phenomenon when $[k_1, k_2]$ are positive. The choice of this particular nonlinear system was prompted by research into the modelling of evoked potentials (EP) [31]. EPs refer to EEG produced as a result of an applied sensory stimulus such as a flashing light or loud tone. The potentials generated in response to such stimuli are the result of synchronous firings of several neuronal clusters; a process that is thought to occur repeatedly in the generation of newborn EEG seizure. There have been several attempts to model EPs, and of particular interest is the application of the Duffing oscillator. The use of this model was first suggested by Zeeman in [36] to analyse the response of the brain, and more recently used to model EPs by Srebo in [31]. Another useful attribute of the Duffing oscillator is that is generates a coloured spectral response when excited by stationary white noise. This colouring approximates the spectrum of newborn EEG background [4], [25].

In the proposed model, we use two Duffing oscillators each with a different excitations, $F(t)$, to simulate newborn EEG seizure and background. Seizure is simulated when the system is driven by a nonstationary impulse train while background is obtained when the system is driven by a stationary white Gaussian noise process. The seizure and background signals are then linearly combined to form simulated newborn EEG,

$$\mathrm{eeg}(t) = k_s(t)\mathrm{seizure}(t) + k_b(t)\mathrm{background}(t) \tag{3}$$

where the gains or modulations, $k_s(t)$ and $k_b(t)$, are used to effectively turn seizure on and off, that is,

$$k_s(t) = \begin{cases} 1 & \text{seizure is present} \\ \\ 0 & \text{when seizure is absent} \end{cases} \tag{4}$$

and,

$$k_b(t) = \begin{cases} k & \text{seizure is present} \\ \\ 1 & \text{when seizure is absent} \end{cases} \tag{5}$$

where, k is a random variable that is uniformly distributed over a seizure to background ratio of 10–30dB, as was used in [6].

The proposed two–component model of newborn EEG is shown in Fig. 3 where the first component models seizure (presented in section III-A) and the second component models background (presented in section III-B).

A. Model of Newborn EEG Seizure

Newborn EEG seizure has been modelled as the output of a linear system driven by a sawtooth waveform, the output of a Wiener system driven by a sawtooth waveform and as an amplitude modulated, multiple component signal with a piecewise linear IF law [6], [25], [27]. In the proposed method, we use a Duffing oscillator driven by a nonstationary impulse train to model newborn EEG seizure.

From a physiological perspective, the seizure waveform is thought to be generated by the repeated, synchronised firing of clusters of neurons [20]. At a neuronal level, significant voltage potential is generated across the membrane of the neuron once the number of excitatory impulses on the neuron exceeds the number of inhibitory impulses by a certain threshold [20]. This voltage potential is transient in nature and can be represented as,

$$\delta(n-n_0)=\begin{cases}1 & n=n_0\\ \\ 0 & \text{elsewhere}\end{cases} \tag{6}$$

where n is discrete time and n_0 is the time shift at which the firing occurs. In the event of an EEG seizure, clusters or populations of neurons fire at approximately the same time (synchronise). The synchronised firings of these neurons repeat at near constant intervals generating an impulse train that can be represented as,

$$\psi(n)=\sum_{i=0}^{N/T}\delta(n-iT), \quad n=[0,...,N-1], \tag{7}$$

where T is the interval between impulses. The frequency domain representation of $\Psi(k)$ is [22],

$$\Psi(k)=\frac{1}{2T}\sum_{i=0}^{T/N}\delta(k-i\tfrac{N}{T}), \quad k=[0,...,N-1], \tag{8}$$

where k is discrete frequency. As can be seen, the frequency domain representation of the impulse train is another impulse train with a period inversely proportional to T. In reality, however, T varies over time, that is we replace iT with $T(i)$ in (7). The time variation in T results in a nonstationary impulse train (an impulse train with time–varying period). This variation between impulses distorts the spectrum of the impulse train. A distortion which becomes even more pronounced when the nonstationary impulse train is modulated in amplitude. This distortion can impede the performance of stationary spectral techniques, such as the Fourier transform, when analysing newborn EEG seizure. Nonstationarity is an important aspect of newborn EEG seizure and it can be used to differentiate between seizure and EEG artifacts, such as those caused by artificial ventilation, which tend to be stationary.

In the proposed model, we define $T(i)$ as,

$$T(i)=T(i-1)+2e(i)T_c, \quad i=[1,...,\mathrm{argmax}_i(T(i)\leq N-1)] \tag{9}$$

where $T(-1)=0$, T_c and $e(i)$ are assumed to be random. The variation in T_c accounts for the different mean frequencies seen in newborn EEG seizure. The incorporation of the random process,

$e(i)$, results in a nonstationary impulse train. The time–varying nature of this impulse train simulate the nonstationary characteristic of newborn EEG seizure which is modelled using piecewise linear functions in the models of Celka and Rankine. We use a random process to model the time–varying behaviour of the impulse train as the subsequent increase in variability is better able to capture the inter–impulse deviation seen in newborn EEG seizure. The increase in variability of the inter–impulse interval also means that a greater number of IF laws are available to represent newborn EEG seizure.

The nonstationary impulse train is not directly recorded by the EEG as it is distorted in the time domain by the latency of synchronisation between, and within, the firing of neuronal clusters that are recruited during seizure; a process which displays nonlinear characteristics [31], [33]. This voltage potential is then further distorted by the transmission of these voltage potentials through the cortex and scalp to the EEG electrode; a process which is commonly assumed to be linear [10]. In terms of modelling newborn EEG seizure, we are not, primarily, interested in modelling these distortions individually but rather the combined effect of these distortions on the EEG. To this end, we use the Duffing oscillator to simulate this process of collective time domain distortion. The response of a Duffing oscillator to an impulse is shown in Fig. 4.

The response of the Duffing oscillator to an impulse has time–varying frequency content that is related to the amplitude envelope of the response (see Fig. 4, where a decrease in signal envelope results in a decrease in signal frequency) and is more suited to the simulation of the synchronised firings seen in EPs than a linear system [31]. It is also capable of generating several different morphologies by varying system parameters, in particular the spike train (system non–resonance) and oscillatory (system resonance) seizures noted in [9] (see Fig. 5). An example of real newborn EEG seizure and a potential output of the proposed seizure model are shown in Fig. 6.

B. Model of Newborn EEG Background

The normal balance between the inhibitory and excitatory influences of the newborn brain result in normal EEG background [16]. This EEG pattern dominates the newborn EEG and can be modelled as a stochastic process with self–similar and nonstationary characteristics [25]. The amplitude of this process is modulated in the short (minutes) and medium (hours) term. The medium term modulation is useful for differentiating between quiet and active sleep in the healthy newborn (such sleep states are not always seen in newborns with seizure), [14]. The short term modulation, associated with discontinuity in the EEG, is useful for prognosis and determining sleep state (burst–suppression has prognostic implications and tracé alternant is used to determine quiet sleep), [18]. The colouring of this spectrum varies on the medium and long term [14], [25], [28]. The long term (years) variation corresponds to a maturation of the newborn brain whereby neuronal feedback is increased due to increasing interconnectivity between neuronal populations which eventually results in the alpha wave pattern seen in the adult [28]. The medium term variation in the spectral colouring can also be used to determine sleep state [14].

Models of newborn EEG background are based on small duration epochs of EEG (< 60s) which are commonly assumed to be stationary. The background EEG has been modelled in the Celka model as an ARMA(10,10) process and as an ARMA(4,2) process in the Roessgen model (both models were driven by stationary white Gaussian noise) [6], [27]. The Rankine model used a time-varying fractional process with an order between 0.5 and 1.5 [25]. All these models produce background that mimics the $1/f$ spectrum typically seen in real newborn EEG [25].

In this paper, we propose a model of newborn EEG background based on driving a Duffing oscillator with stationary white Gaussian noise. The output of the Duffing oscillator when excited by white Gaussian noise can be approximated using statistical linearisation as [4],

$$S(\omega) = \frac{2d}{(\gamma^2 - \omega^2)^2 + \omega^2 c^2} \tag{10}$$

where d and γ are averaged quantities related to the linearisation of the nonlinearity. This is essentially a second order AR process. We can incorporate longer term nonstationary behaviour into the background model by varying the parameters of the Duffing oscillator over time and by modulating the background using $k_b(t)$. An example output of the newborn EEG background model is plotted along with an epoch of real newborn EEG background in Fig. 7.

IV. Model Parameter Estimation, Comparison and Validation

The proposed model was compared to the models of Roessgen *et al.* [27], Celka and Colditz [6] and Rankine *et al.* [25] using a database of real newborn EEG. The models were compared by estimating the linear correlation coefficient between real epochs of EEG and potential outputs of each model. The potential model outputs were generated using values for the model input and system parameters that were directly estimated from the real epoch of EEG. The coefficient was estimated in the time domain for comparing seizure models and in the frequency domain for comparing background models. The time domain was used to assess the seizure model as the ability of the model to accurate represent seizure morphology was paramount. The frequency domain, via an estimate of the power spectral density (PSD), was used to assess the background model as the background was assumed to be a coloured stochastic process. The PSD was estimated using Welch's periodogram with a window of 64 samples and an overlap of 32 samples [35].

The proposed model uses randomly distributed parameters in order to represent the variability of the EEG waveforms over time and with respect to the diversity of patients who experience seizure. The validity of assuming randomly distributed parameters was tested using a 4–fold cross–validation process to test the distribution of the model parameters across subsets of the data. The database of newborn EEG was segmented into 8 subsets (4 seizure and 4 background) and the distribution of each parameter was compared, within sub–models, across subsets using a nonparametric Kolmogorov–Smirnov test [8]. The null hypothesis was that the parameters of the two subsets under test were drawn from the same underlying distribution.

A. Newborn EEG Seizure Model

The analysis of the newborn EEG seizure model used 200, 8s epochs of newborn EEG seizure (an epoch length of 256 samples). The parameters to be estimated for the model comparison include $[c,\ k_2, T_c, e(i)]$ from (1), (2) and (9) where $m = 1$ and $k_1 = 0$ to lessen the computation burden on the model identification algorithm. Parameter m was set to be constant as it primarily affects the gain of the system and the linear component of $g(x(t))$ was set to zero as we were primarily interested in the effect of the nonlinear aspects of the model. Preliminary analysis showed negligible improvement was achieved from incorporating k_1.

All newborn EEG seizure models (except for the Rankine model) were driven by an input with an IF law estimated directly from the signal using the peak extraction algorithm outlined in [19]. The peak localisation process uses a short–time average generated by passing the EEG epoch through the following filter,

$$H(z) = \frac{1}{\tau f_s - (\tau f_s - 1)\, z^{-1}} \tag{11}$$

where f_s is the sampling frequency (32Hz) and τ is a time constant (1 sec). This short–time mean is then offset by a value that is half the difference between the mean and maximum voltage of the EEG epoch. The EEG epoch is then segmented, using the intersections between the short–time average and the EEG, and then searched for the largest local maxima. The location of these maxima were used to generate the impulse train waveform and sawtooth waveform inputs for the models under test. The epoch–dependent determination of the IF of the input was incorporated into these models for more accurate comparison.

This input was applied to the Duffing oscillator and the parameters were iteratively varied until the minimum square error between the oscillator output and the newborn EEG seizure epoch was reached (Levenberg-Marquardt minimisation) [26]. The Duffing oscillator was solved numerically using a Dormand–Prince tableau with fixed step size [30]. The ARMA models used in [27] and [6] were estimated using the ARMAX function from the system identification toolbox in Matlab (The Mathworks, Inc., USA) using a sawtooth input. The polynomial form of the nonlinear mapping of the Wiener model was given in [6] and the polynomials were estimated using the POLYFIT function in Matlab. The Celka model used a single nonlinear mapping function as a model for newborn EEG seizure. We used an epoch–dependent nonlinear mapping function for more accurate comparison. The amplitude modulation and IF law of the signal components used in the model outlined in [25] were estimated directly from the spectrogram of the EEG epoch using an edge–linking algorithm [24].

The use of epoch–dependent nonstationary inputs and epoch–dependent nonlinear mapping functions in the models of Roessgen and Celka constitutes an improvement to these models and resulted in optimised representations of each epoch of newborn EEG seizure data under analysis.

Once the ARMA, Wiener and Duffing oscillators were identified, simulated epochs of newborn EEG seizure were generated. The parameters used in each model and the linear correlation coefficient between potential outputs of the various newborn EEG seizure models and real epochs of newborn EEG seizure are shown in Table I (note, the Roessgen and Celka models have been optimised to improve their performance). The results show that the proposed model uses fewer parameters than currently available models and results in outputs that are more highly correlated with newborn EEG seizure.

The parameters used in the newborn EEG seizure model were assumed to be randomly distributed. The validity of this assumption was tested using 4-fold cross-validation (6 trials) with a Kolmogorov–Smirnov test [8]. The newborn EEG seizure database was split into 4 subsets of 50 epochs and the parameters estimated from each subset were tested against each other to see if they were drawn from the same underlying distribution. The results presented in Table II show that the distributions of the newborn EEG seizure model parameters did not change significantly across 4 independent subsets of newborn EEG seizure.

The distribution of each parameter was modelled with the Beta distribution [23]. We used the Beta distribution as it is a bounded, adaptable distribution that can cope with limits on the EEG signals due to filtering and sampling. The limit on $f_c = 1/T_c \sim [0.5, f_s/2]$; the limits on $[k_2, c]$ are less well defined, but are related to the frequency content of the Duffing oscillator and, therefore, are affected by sampling. The validity of using a Beta distribution to represent each parameter was tested using a Kolmogorov–Smirnov test. The distribution of T_c (expressed as a frequency $f_c = 1/T_c$) and $e(i)$ are shown in Fig. 8. The joint distribution of the nonlinear spring constant and damping coefficient is shown in Fig. 9(a). The use of joint distributions was necessary as the frequency content of the Duffing oscillator is jointly related to both the effective spring constant and damping value. The joint distribution was modelled as a two–dimensional Beta distribution which was estimated using a two–dimensional histogram. The 25%, 50% and 75% percentiles of each parameter are presented in Table III.

B. Newborn EEG Background Model

The analysis of the newborn EEG background model used 2000, 8s epochs of newborn EEG background (an epoch length of 256 samples). In an attempt to use similar model identification processes we assumed the spectral response of the Duffing oscillator to white noise was an AR(2) process, as per the linearised model in (10). We estimated the ARMA coefficients of each model, using the ARMAX and ARX functions in Matlab, and then averaged these values to construct an average spectral response. This average spectral response was then compared to the spectral response of 2000 epochs of newborn EEG background using the correlation coefficient. The background model of [25] was estimated using Higuchi's estimate of the fractal dimension which has been shown to be effective when using short lengths of data [13]. The parameters used in each model and the linear correlation coefficient between the average model spectrum and EEG background spectra are shown in Table IV. These correlation values can be interpreted as measures of the variance between the spectrum of an optimal background model and 2000 realisations of newborn EEG. The results show the proportional relationship seen between correlation and model parameter number, with the proposed model offering the third highest correlation value.

The parameters used in the newborn EEG background model were assumed to be randomly distributed. The validity of this assumption was tested using 4–fold cross–validation (6 trials) with a Kolmogorov–Smirnov test [8]. The newborn EEG background database was split into 4 subsets of 500 epochs and the parameters estimated from each subset were tested against each other to see if they were drawn from the same underlying distribution. The results presented in Table V show that the distributions of the newborn EEG background model parameters did not change significantly across 4 independent subsets of newborn EEG background.

The model parameters were modelled with Beta distributions. The joint distribution of the nonlinear spring constant and damping coefficient is shown in Fig. 9(b). The parameters used in the background Duffing oscillator were selected to minimise the least square error between estimates of the spectrum of the Duffing oscillator, excited by 25 realisations of white Gaussian noise, and the spectrum of 2000 real background epochs. The 25%, 50% and 75% percentiles of each parameter are presented in Table VI.

V. Simulation

The simulation of newborn EEG, using the proposed model, involves randomly selecting the parameters of the seizure and background model components, from relevant distributions, and then exciting each model component with white noise to simulate newborn EEG background or a randomly generated nonstationary impulse train to simulate newborn EEG seizure. The block diagram for the newborn EEG simulation algorithm is shown in Fig. 10. The parameters used in the seizure and background Duffing oscillators, and drawn from the distributions shown in Figs. 8 and 9. The simulation algorithm is available at http://www.ucc.ie/en/neonatalbrain/. An example epoch of simulated newborn EEG is shown in Fig. 11. The proposed model generates simulated newborn EEG signals with desirable signal characteristics, notably a coloured stochastic background and a seizure waveform that is nonstationary with evolving morphology.

VI. Discussion

The seizure waveform recorded by the EEG is generated by the repeated synchronised firings of localised neuronal populations. This synchronisation may not be perfect and it can be assumed that there will be delays between the synchronised firing of nearby neuronal populations. The delay in synchronisation can be simulated by a high order linear system or a low order nonlinear system. The advantage of using a low order nonlinear dynamic system is a simpler model that is capable of incorporating additional nonlinear effects of the process. Variation in the delay, which relates to the plasticity of the brain region and even the geometry of local neuronal populations with respect to the electrode, results in different seizure waveform morphologies. This suggests that the morphology of the seizure waveform may be able to provide information on the extent or location of the injury.

The use of a sawtooth waveform causes difficulties in the Roessgen and Celka model that are only overcome by using many parameters and unstable transfer functions in their respective models. The use of a sawtooth waveform was motivated by the need to generate harmonics that could be shaped via ARMA filters to more accurately model seizure morphology in the time domain. A nonlinear mapping was introduced in the Celka model to improve the morphology of the simulated seizure waveform. The Celka model, however, requires the selection of 48 parameters to define the Wiener systems used for simulating an epoch of newborn EEG. An improvement over this model can be made by using a nonlinear dynamic system which is more capable of capturing various seizure morphologies than a constant nonlinear function. In addition, the use of an impulse train input generates a spectral response that is more amenable to colouring via filtering. This means that an equivalent epoch of newborn EEG can be simulated by defining just 4 parameters of the Duffing oscillator with improved accuracy.

The similarities between the proposed model and an LPC speech coder suggest that various techniques that have been developed for differentiating between voiced and unvoiced speech can also be applied to the problem of newborn EEG seizure detection [32]. The major differences between the two applications are the higher occurrence of voiced speech compared to seizure in a recording, a lower signal to noise ratio in EEG recordings and the requirement of stricter performance criteria for the seizure detection problem.

The definition and development of a model of newborn EEG suggests the application of system identification techniques to the seizure detection problem. Model based seizure detectors have been applied in the past with limited success (see [11], [27]). The idea of using model based features to simplify the detection problem such as whitening the data with a nonlinear (or linear approximation) filter, however, appeal. The use of whitening simplifies the seizure detection problem to the task of detecting a nonstationary impulse train in white noise. Recent advances in sampling nonstationary, impulsive signals that have a finite rate of innovation may result in optimal detection strategies for such signals [34]. The pre–whitening of EEG was initially used in the detection algorithm of Celka and Colditz in [7] and has been largely ignored in subsequent algorithms.

The identification of newborn EEG seizure as a nonlinear, repetitive deterministic waveform emerging from a stochastic background suggests the use of higher order spectra for analysis [3]. The ability of higher–order spectra to identify nonlinear coupling in repetitive waveforms while rejecting Gaussian noise appears highly suited to the newborn EEG seizure detection problem.

The impulse train used as the input (or perturbation) of our seizure model is well known in the analysis of linear time–invariant systems. The impulse response of a linear time–invariant system completely defines the system. The concept of perturbing a system and monitoring its response has been clinically applied in EPs. As a result, the analysis of EPs has been used for the diagnosis of the CNS. If we assume that the repetitive synchronised firings of neurons that make up the seizure waveform can be considered as a sequence of EPs, then the analysis of the seizure waveform may provide useful information as to the functioning of the brain which, in turn, has clear diagnostic implications.

To the best of the author's knowledge, this is the first attempt at providing a system based model of newborn EEG where the range and distribution of the input and system parameters have been defined based on a database of newborn EEG. The proposed model uses Duffing oscillators with random, but constrained, parameters driven by stationary and nonstationary inputs to represent a database of newborn EEG seizure and background waveforms. A more complete model would include simulation of other deterministic patterns commonly seen in the neonatal EEG, an attempt to incorporate longer term dynamics (by varying model parameters slowly over time) or amplitude modulations (such as sleep states) and the generation of multiple channel EEG data.

VII. Conclusion

We propose a new model of newborn EEG based on a second order nonlinear differential equation, under different excitations, to simulate different components of newborn EEG. This system when driven by stationary random noise simulates background EEG and when driven by a nonstationary impulse train simulates seizure EEG. The seizure model is based on the interpretation of the seizure as a sequence of internally evoked potentials. This form of nonlinear system also shapes the spectrum of a random noise process with a inverse power law relationship which has been shown to be a characteristic of newborn EEG background. The behaviour of this model also has useful connotations for automatic seizure detection algorithms. The proposed model accounted for 54% of the linear variation in the time domain, for seizure, and 85% of the linear variation in the frequency domain, for background, of a database of newborn EEG. This constitutes an improvement in combined performance of 6%, with a reduction from 48 to 4 model parameters, compared to an optimised implementation of the Celka model.

VIII. Reproducible Research

The database of 200 seizure epochs and 2000 artifact free background epochs, the Matlab m-files used throughout this paper and the newborn EEG simulator are available at http://www.ucc.ie/en/neonatalbrain.

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IX. Figure Captions

1) An general outline of the significant components that define the structure of newborn EEG.
2) The time domain and frequency domain representation of 8s epochs of newborn EEG seizure and background, the EEG recordings are in microvolts (μV).
3) An interpretation of the general outline of newborn EEG that is of interest when developing methods for newborn EEG seizure detection.
4) The response of the Duffing oscillator and a linear system to a unit impulse function.
5) The types of newborn EEG seizure morphology that can be simulated by the Duffing oscillator, (a) is a overdamped Duffing (sawtooth) seizure, (b) is a critically damped Duffing seizure, (c) is an underdamped Duffing seizure (the most common form of seizure), and (d) is the resonant Duffing seizure (typically seen at the start of a seizure event).
6) Newborn EEG seizure and a potential output of the newborn EEG seizure model ($m = 1, c = 5.1, k_1 = 0, k_2 = 10^{6.8}$).
7) Newborn EEG background and a potential output of the newborn EEG background model ($m = 1, c = 306, k_1 = 0, k_2 = 10^{2.2}$).
8) The distribution of the parameters used to construct the impulse train input for the seizure model. $p(f_c) = \mathrm{Beta}(1.28, 3.04)$ and $p(e) = \mathrm{Beta}(10.97, 11.00)$
9) The joint distribution of the parameters of the Duffing oscillator used to simulate newborn EEG, where $\bullet$ denotes the maximum.
10) The algorithm for simulating newborn EEG using the proposed model. The numbers in brackets relate to equations from the text and the figures referred to depict the distribution that the parameters are randomly selected from.
11) An example simulation of newborn EEG using the proposed model.

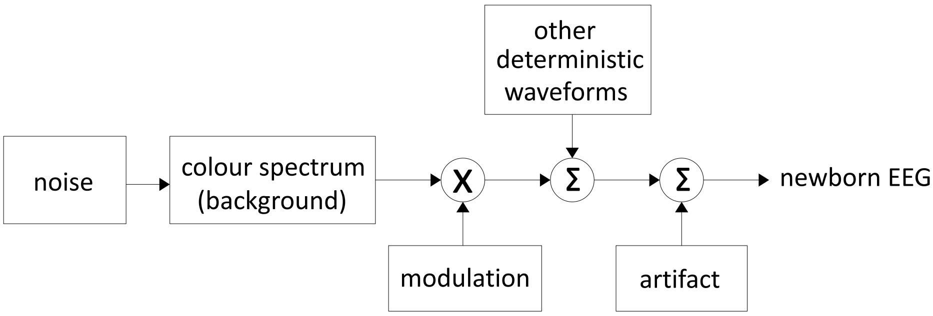
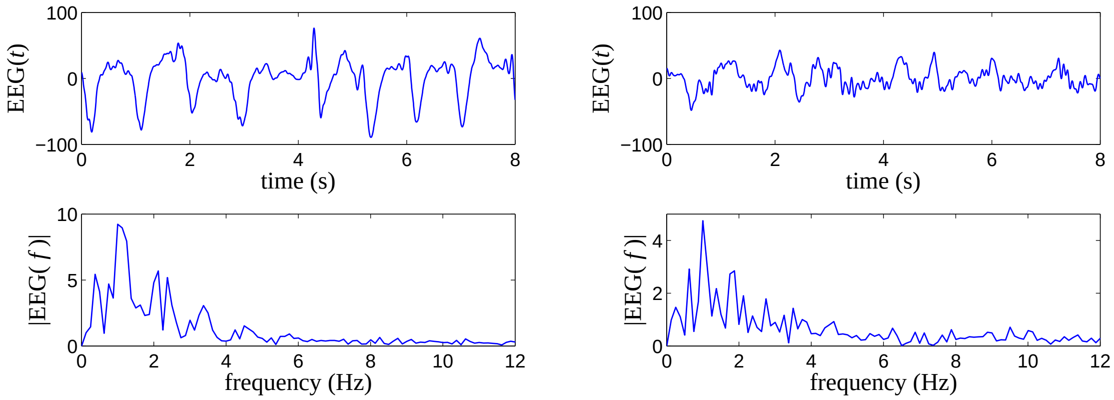
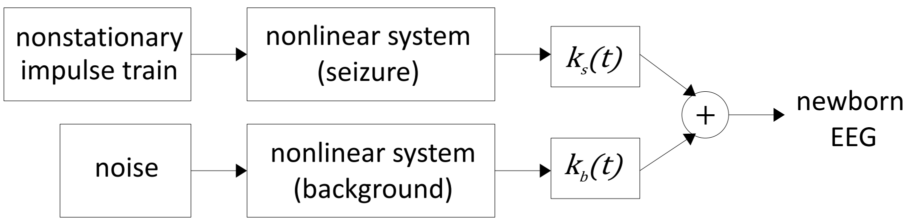


Fig. 1.



(a) seizure (b) background

Fig. 2.



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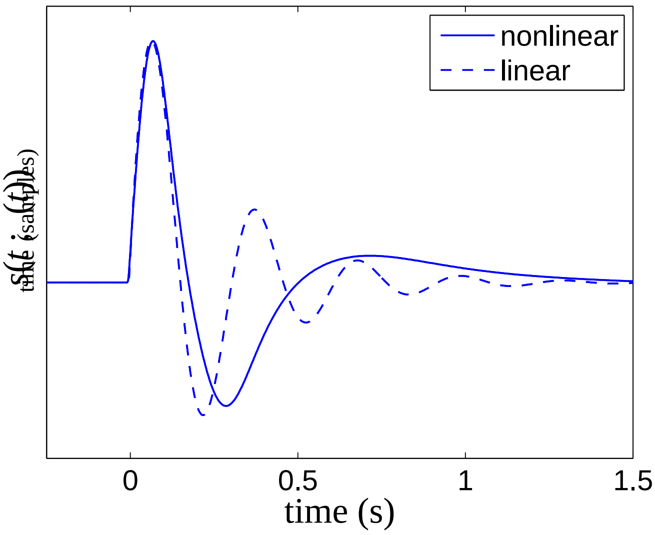

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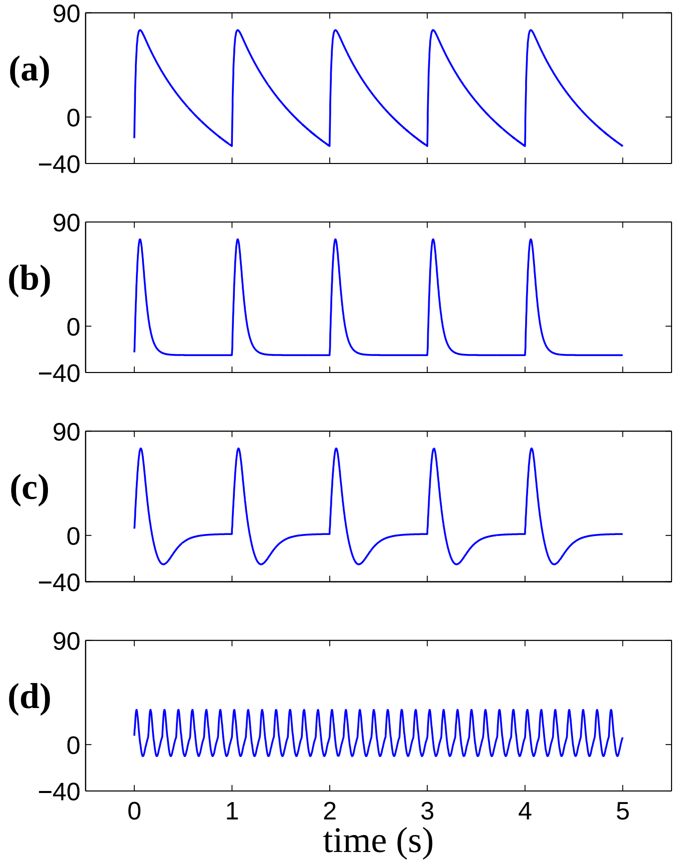


Fig. 5.

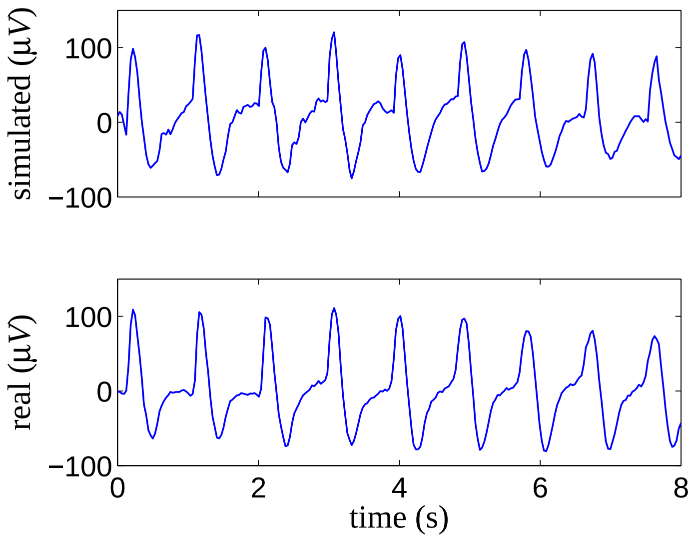

simulated (μV)
100
0
−100
real (μV)
100
0
−100
0
2
4
6
8
time (s)

Fig. 6.

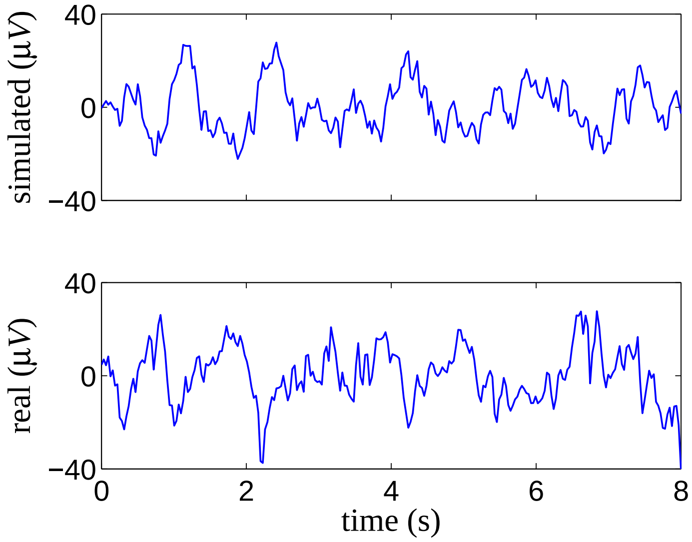
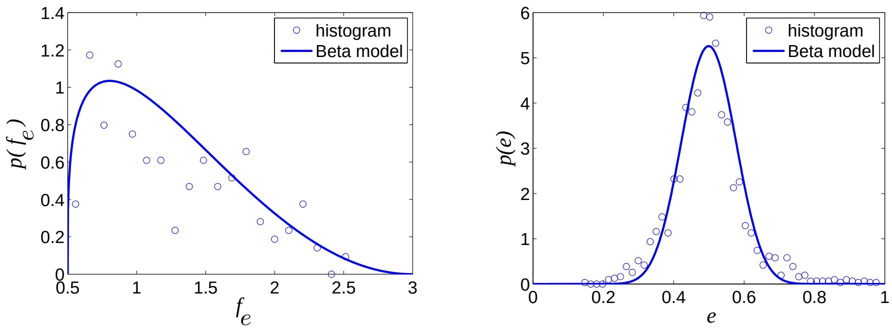
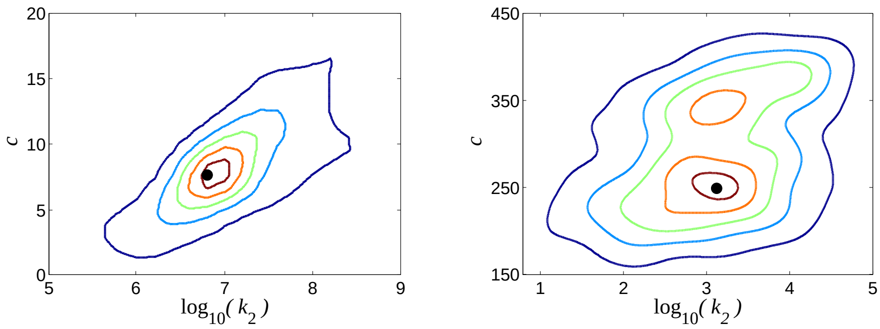

simulated (μV)
40
0
−40
real (μV)
40
0
−40
0
2
4
6
8
time (s)

Fig. 7.



(a) $p(f_c)$ (b) $p(e)$

Fig. 8.



(a) seizure (b) background

Fig. 9.

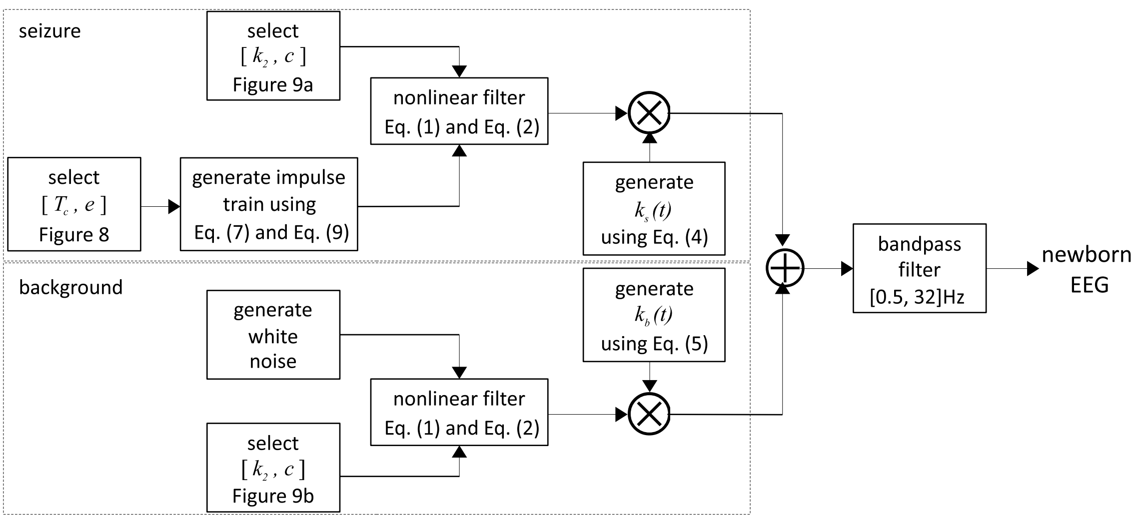


Fig. 10.

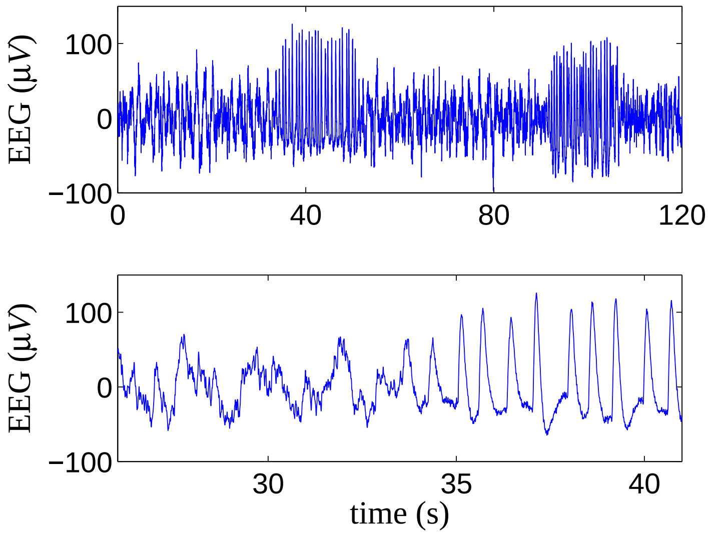


Fig. 11.

TABLE I

THE CORRELATION COEFFICIENT BETWEEN SIMULATED AND REAL EPOCHS ON NEWBORN EEG SEIZURE AND, A LIST OF PARAMETERS USED THE MODEL. THE RESULTS ARE PRESENTED IN THE FORM, MEAN (STANDARD DEVIATION), OF 200 EPOCHS OF NEWBORN EEG SEIZURE AND †DENOTES SIGNIFICANTLY LOWER VALUES (5% LEVEL IN A MANN–WHITNEY U TEST) COMPARED TO THE PROPOSED MODEL.

	parameters	ρ in time	ρ^2
Roessgen†	$[T_c, e, \mathrm{ARMA}(4,2)]$	0.609 (0.128)	0.371
Celka†	$[T_c, e, \mathrm{ARMA}(10,10), g_s]$	0.663 (0.110)	0.440
Rankine†	$[K, R, V_n, P, M, \psi, B, f_{st}, \sigma_k]$	0.455 (0.106)	0.207
Duffing oscillator	$[T_c, e, k_2, c]$	0.732 (0.095)	0.536

TABLE II

THE AVERAGE p–VALUE AND NUMBER OF TIMES THE NULL HYPOTHESIS WAS REJECTED WHEN COMPARING PARAMETER DISTRIBUTIONS OF THE NEWBORN EEG SEIZURE MODEL ACROSS DATA SUBSETS.

parameters	p–value	rejections
k_2	0.41	0
c	0.61	0
T_c	0.46	0
$e(i)$	0.40	0

TABLE III

THE QUARTILES OF THE FOUR PARAMETERS USED TO SIMULATE NEWBORN EEG SEIZURE.

parameters	25% Quartile	50% Quartile	75% Quartile
$\log_{10}(k_2)$	6.717	7.003	7.430
c	6.539	8.491	10.754
T_c	0.607	0.887	1.206
$e(i)$	0.443	0.495	0.545

TABLE IV

THE CORRELATION COEFFICIENT BETWEEN SIMULATED AND REAL EPOCHS ON NEWBORN EEG BACKGROUND AND, A LIST OF PARAMETERS USED THE MODEL. THE RESULTS ARE PRESENTED IN THE FORM, MEAN (STANDARD DEVIATION), OF 2000 EPOCHS OF NEWBORN EEG BACKGROUND AND †AND ‡DENOTE SIGNIFICANTLY LOWER AND HIGHER VALUES (5% LEVEL IN A MANN–WHITNEY U TEST) RESPECTIVELY, COMPARED TO THE PROPOSED MODEL.

	parameters	ρ in frequency	ρ^2
Roessgen‡	$[\mathrm{ARMA}(4,2)]$	0.939 (0.037)	0.882
Celka‡	$[\mathrm{ARMA}(10,10), g_b]$	0.941 (0.042)	0.886
Rankine†	$[H]$	0.872 (0.071)	0.760
Duffing oscillator	$[\mathrm{AR}(2)]$	0.921 (0.039)	0.848

TABLE V

THE AVERAGE p–VALUE AND NUMBER OF TIMES THE NULL HYPOTHESIS WAS REJECTED WHEN COMPARING PARAMETER DISTRIBUTIONS OF THE NEWBORN EEG BACKGROUND MODEL ACROSS DATA SUBSETS.

parameters	p–value	rejections
k_2	0.42	0
c	0.65	0

TABLE VI

THE QUARTILES OF THE TWO PARAMETERS USED TO SIMULATE NEWBORN EEG BACKGROUND.

parameters	25% quartile	50% quartile	75% quartile
$\log_{10}(k_2)$	1.477	2.222	3.443
c	302.78	335.00	363.91